142-LIPS

Pentachlorophenol-Induced Stimulation of IL-6 Production by Human Immune Cells Relies on MyD88

Pentachlorophenol (PCP) contaminates the environment due to its use as a biocidal agent. It is detected in human blood samples at levels as high as 5 μM. PCP exposure has been associated with certain cancers, including multiple myeloma and kidney cancer. Interleukin-6 (IL-6) is a pro-inflammatory cytokine produced by immune cells in response to pathogen- or damage-associated molecular patterns (PAMPS/DAMPS) activation of toll-like receptors (TLRs) Stimulation of IL-6 production in the absence of an appropriate signal can lead to chronic inflammation, which can result in cancer development and/or progression. PCP has been shown to stimulate inappropriate production of IL-6 and this stimulation is at least in part dependent on TLR-4 and TLR-8. Both TLR-4 and TLR-8 are linked to the intracellular adapter MyD88 which is part of the pathway that leads to cellular production of IL-6 and other pro-inflammatory cytokines. In this study the hypothesis that MyD88 activity is needed for PCP to stimulate immune cell production of IL-6 is tested. Immune cells were treated with a selective inhibitor of MyD88 prior to exposure to PCP. Cellular production of IL-6 was monitored using ELISA for secreted levels of IL-6 and western blot for intracellular IL-6. The results indicate that PCP-induced stimulation of IL-6 production was either completely blocked or greatly diminished in immune cells where MyD88 was inhibited. These results further elucidate the mechanism by which PCP can lead to very significant elevations of IL-6, which has the potential to produce chronic inflammation. This PCP induced inflammation may, at least partially, be responsible for the noted association of PCP exposures with the development of several cancers.